(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
20 January 2005 (20.01.2005)

PCT

(10) International Publication Number
WO 2005/004911 A2

(51) International Patent Classification[7]: A61K 39/39, 39/04, A61P 31/06

(21) International Application Number: PCT/DK2004/000488

(22) International Filing Date: 7 July 2004 (07.07.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
PA 2003 01046 9 July 2003 (09.07.2003) DK
PA 2003 01403 27 September 2003 (27.09.2003) DK

(71) Applicant *(for all designated States except US)*: **STATENS SERUM INSTITUT** [DK/DK]; Artillerivej 5, DK-2300 Copanhagen S (DK).

(72) Inventors; and

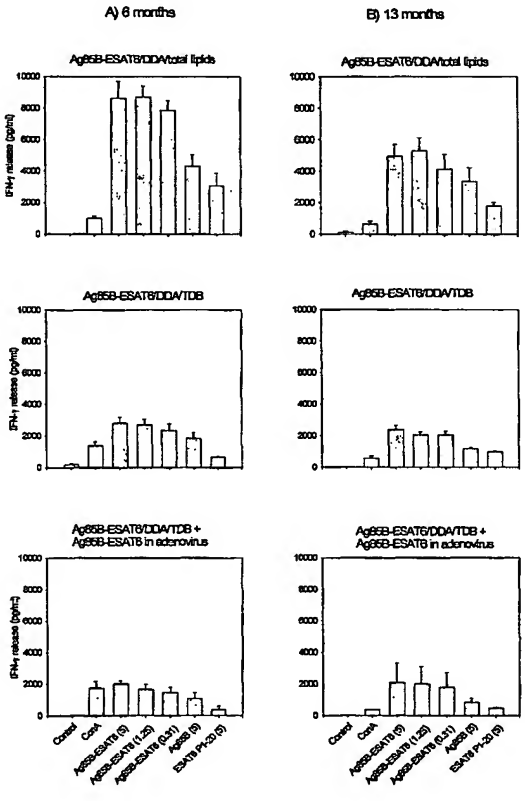
(75) Inventors/Applicants *(for US only)*: **AGGER, Else, Marie** [DK/DK]; Krudtmøllegårds Allé 9, DK-2300 Copenhagen S (DK). **ANDERSEN, Peter** [DK/DK]; Sparreholmvej 47, DK-2700 Brønshøj (DK). **OLSEN, Anja** [DK/DK]; Jacob Bulls Allé 121, DK-2860 Søborg (DK). **ROSENKRANDS, Ida** [DK/DK]; Kastaniehaven 9, DK-3500 Værløse (DK).

(74) Common Representative: **TOFT, Lars**; Statens Serum Institut, Corporate Affairs, Artillerivej 5, DK-2300 Copenhagen S (DK).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,

[Continued on next page]

(54) Title: ADJUVANT COMBINATIONS OF LIPOSOMES AND MYCOBACTERIAL LIPIDS FOR IMMUNIZATION COMPOSITIONS AND VACCINES



(57) Abstract: The present invention provides a vaccine adjuvant consisting of a combination of a surfactant i.e. dimethyldeoctadecylammonium-bromide/chloride (DDA) and a lipid extract from *Mycobacterium bovis* BCG. The total lipid extract contains both apolar lipids, polar lipids, and lipids of intermediate polarity of which the apolar lipids were found to induce the most powerful immune responses. The total lipids may be extracted with chloroform/methanol and re-dissolved in water before the addition of surfactant. This preparation may be used to induce prominent cell-mediated immune responses in a mammal in order to combat pathogens, or as a treatment for cancer.

WO 2005/004911 A2

TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) **Designated States** *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declaration under Rule 4.17:
— *of inventorship (Rule 4.17(iv)) for US only*

Published:
— *without international search report and to be republished upon receipt of that report*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
20 January 2005 (20.01.2005)

PCT

(10) International Publication Number
WO 2005/004911 A3

(51) International Patent Classification[7]: A61K 39/39, 39/04, A61P 31/06

(21) International Application Number: PCT/DK2004/000488

(22) International Filing Date: 7 July 2004 (07.07.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
PA 2003 01046 9 July 2003 (09.07.2003) DK
PA 2003 01403 27 September 2003 (27.09.2003) DK

(71) Applicant *(for all designated States except US)*: **STATENS SERUM INSTITUT** [DK/DK]; Artillerivej 5, DK-2300 Copanhagen S (DK).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **AGGER, Else, Marie** [DK/DK]; Krudtmøllegårds Allé 9, DK-2300 Copenhagen S (DK). **ANDERSEN, Peter** [DK/DK]; Sparreholmvej 47, DK-2700 Brønshøj (DK). **OLSEN, Anja** [DK/DK]; Jacob Bulls Allé 121, DK-2860 Søborg (DK). **ROSENKRANDS, Ida** [DK/DK]; Kastaniehaven 9, DK-3500 Værløse (DK).

(74) Common Representative: **TOFT, Lars**; Statens Serum Institut, Corporate Affairs, Artillerivej 5, DK-2300 Copenhagen S (DK).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declaration under Rule 4.17:
— *of inventorship (Rule 4.17(iv)) for US only*

Published:
— *with international search report*
— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

(88) Date of publication of the international search report: 17 February 2005

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: ADJUVANT COMBINATIONS OF LIPOSOMES AND MYCOBACTERIAL LIPIDS FOR IMMUNIZATION COMPOSITIONS AND VACCINES

(57) Abstract: The present invention provides a vaccine adjuvant consisting of a combination of a surfactant i.e. dimethyldioctadecylammonium-bromide/chloride (DDA) and a lipid extract from The present invention provides a vaccine adjuvant consisting of a combination of a surfactant i.e. dimethyldeoctadecylammonium-bromide/chloride (DDA) and a lipid extract from <The present invention provides a vaccine adjuvant consisting of a combination of a surfactant i.e. dimethyldeoctadecylammonium-bromide/chloride (DDA) and a lipid extract from *Mycobacterium bovis. The present invention provides a vaccine adjuvant consisting of a combination of a surfactant i.e. dimethyldeoctadecylammonium-bromide/chloride (DDA) and a lipid extract from Mycobacterium bovis <The present invention provides a vaccine adjuvant consisting of a combination of a surfactant i.e. dimethyldeoctadecylammonium-bromide/chloride (DDA) and a lipid extract from Mycobacterium bovis BCG The present invention provides a vaccine adjuvant consisting of a combination of a surfactant i.e. dimethyldeoctadecylammonium-bromide/chloride (DDA) and a lipid extract from Mycobacterium bovis BCG<The present invention provides a vaccin adjuvant consisting of a combination of a surfactant i.e. dimethyldeoctadecylammonium-bromide/chloride (DDA) and a lipid extract from Mycobacterium bovis BCG. The present invention provides a vaccine adjuvant consisting of a combination of a surfactant i.e. dimethyldeoctadecylammonium-bromide/chloride (DDA) and a lipid extract from <i>Mycobacterium bovis BCG<i>. <The present invention provides a vaccine adjuvant consisting of a combination of a surfactant i.e. dimethyldeoctadecylammonium-bromide/chloride (DDA) and a lipid extract from <i>Mycobacterium bovis BCG<i>.* The total lipid extract contains both apolar lipids, polar lipids, and lipids of intermediate polarity of which the apolar lipids were found to induce the most powerful immune responses. The total lipids may be extracted with chloroform/methanol and re-dissolved in water before the addition of surfactant. This preparation may be used to induce prominent cell-mediated immune responses in a mammal in order to combat pathogens, or as a treatment for cancer.

WO 2005/004911 A3

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
20 January 2005 (20.01.2005)

PCT

(10) International Publication Number
WO 2005/004911 A3

(51) International Patent Classification[7]: A61K 39/39, 39/04, A61P 31/06

(21) International Application Number: PCT/DK2004/000488

(22) International Filing Date: 7 July 2004 (07.07.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
PA 2003 01046 9 July 2003 (09.07.2003) DK
PA 2003 01403 27 September 2003 (27.09.2003) DK

(71) Applicant *(for all designated States except US)*: **STATENS SERUM INSTITUT** [DK/DK]; Artillerivej 5, DK-2300 Copanhagen S (DK).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **AGGER, Else, Marie** [DK/DK]; Krudtmøllegårds Allé 9, DK-2300 Copenhagen S (DK). **ANDERSEN, Peter** [DK/DK]; Sparreholmvej 47, DK-2700 Brønshøj (DK). **OLSEN, Anja** [DK/DK]; Jacob Bulls Allé 121, DK-2860 Søborg (DK). **ROSENKRANDS, Ida** [DK/DK]; Kastaniehaven 9, DK-3500 Værløse (DK).

(74) Common Representative: **TOFT, Lars**; Statens Serum Institut, Corporate Affairs, Artillerivej 5, DK-2300 Copenhagen S (DK).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declaration under Rule 4.17:
— *of inventorship (Rule 4.17(iv)) for US only*

Published:
— *with international search report*
— *with amended claims*

(88) Date of publication of the international search report: 17 February 2005

Date of publication of the amended claims: 17 March 2005

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: ADJUVANT COMBINATIONS OF LIPOSOMES AND MYCOBACTERIAL LIPIDS FOR IMMUNIZATION COMPOSITIONS AND VACCINES

(57) Abstract: The present invention provides a vaccine adjuvant consisting of a combination of a surfactant i.e. dimethyldioctadecylammonium-bromide/chloride (DDA) and a lipid extract from The present invention provides a vaccine adjuvant consisting of a combination of a surfactant i.e. dimethyldeoctadecylammonium-bromide/chloride (DDA) and a lipid extract from <The present invention provides a vaccine adjuvant consisting of a combination of a surfactant i.e. dimethyldeoctadecylammonium-bromide/chloride (DDA) and a lipid extract from *Mycobacterium bovis. The present invention provides a vaccine adjuvant consisting of a combination of a surfactant i.e. dimethyldeoctadecylammonium-bromide/chloride (DDA) and a lipid extract from Mycobacterium bovis <The present invention provides a vaccine adjuvant consisting of a combination of a surfactant i.e. dimethyldeoctadecylammonium-bromide/chloride (DDA) and a lipid extract from Mycobacterium bovis BCG The present invention provides a vaccine adjuvant consisting of a combination of a surfactant i.e. dimethyldeoctadecylammonium-bromide/chloride (DDA) and a lipid extract from Mycobacterium bovis BCG<The present invention provides a vaccin adjuvant consisting of a combination of a surfactant i.e. dimethyldeoctadecylammonium-bromide/chloride (DDA) and a lipid extract from Mycobacterium bovis BCG. The present invention provides a vaccine adjuvant consisting of a combination of a surfactant i.e. dimethyldeoctadecylammonium-bromide/chloride (DDA) and a lipid extract from <i>Mycobacterium bovis BCG<i>. <The present invention provides a vaccine adjuvant consisting of a combination of a surfactant i.e. dimethyldeoctadecylammonium-bromide/chloride (DDA) and a lipid extract from <i>Mycobacterium bovis BCG<i>.* The total lipid extract contains both apolar lipids, polar lipids, and lipids of intermediate polarity of which the apolar lipids were found to induce the most powerful immune responses. The total lipids may be extracted with chloroform/methanol and re-dissolved in water before the addition of surfactant. This preparation may be used to induce prominent cell-mediated immune responses in a mammal in order to combat pathogens, or as a treatment for cancer.

WO 2005/004911 A3